U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON ENERGY AND COMMERCE

December 6, 2019

TO: Republican Members, Committee on Energy and Commerce

FROM: Committee Republican Staff

RE: Hearing entitled "Securing the U.S. Drug Supply Chain: Oversight of FDA's Foreign Inspection Program"

The Subcommittee on Oversight and Investigations will hold a hearing on Tuesday, December 10, 2019, at 10:00 a.m. in 2123 Rayburn House Office Building entitled "Securing the U.S. Drug Supply Chain: Oversight of FDA's Foreign Inspection Program."

I. WITNESSES

- Mary Denigan-Macauley, Ph.D., Director, Health Care, U.S. Government Accountability Office; and
- Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration.

II. BACKGROUND

A. Overview of FDA Foreign Drug Inspection Program

Most drugs and drug ingredients used by American consumers are made overseas. The Food and Drug Administration (FDA) reported that in 2018, 88 percent of the manufacturing sites making active pharmaceutical ingredients (APIs) and 63 percent of sites making finished dosage forms (FDFs) were located overseas.[1] India and China manufacture at least 45 percent of APIs for drugs made in the United States.[2] While India is a large manufacturer of finished products for the U.S. and supplies nearly one-quarter of all FDFs, India imports approximately 80 percent of their APIs from China.[3]

The FDA is responsible for overseeing the safety and effectiveness of all drugs marketed in the United States under the Federal Food, Drug, and Cosmetic Act (FFDCA).

[1] U.S. Food & Drug Admin. (FDA), *Drug Shortages: Root Causes and Potential Solutions*, (2019), *available at* https://www.fda.gov/media/131130/download.
[2] *Id*. These numbers apply to manufacturers named in approved applications. Medical gas, compounding, pending application and non-application (OTC) facilities are excluded.
[3] Deepak Patel, *Pharma Sector: 80 per Cent APIs via Chinese Imports despite Similar Making Costs*, (June 9, 2018), *available at* https://indianexpress.com/article/business/business-others/pharma-sector-80-per-cent-apis-via-chinese-imports-despite-similar-making-costs-5222951/.

Inspection Authorities

The FFDCA requires establishments engaged in the manufacture, preparation, propagation, compounding, or processing of human or veterinary drugs, human biological products, and devices to register and submit a listing of every product in commercial distribution to FDA. Section 704(a) of the FFDCA gives the FDA authority to conduct inspections, specifically authorizing duly appointed employees of the FDA or designated officers to enter and inspect, at reasonable times, within reasonable limits and in a reasonable manner, facilities under the jurisdiction of the FFDCA.[4] In FY 2005, FDA implemented a risk based approach to prioritizing human drug manufacturing sites for routine Current Good Manufacturing Practice (CGMP) surveillance inspections, which replaced the biennial inspection frequency for domestic facilities, previously established in section 510(h) of the FFDCA.[5] The FFDCA did not provide a fixed schedule for inspection of foreign facilities.

In July 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) (Public Law 112-144) was signed into law. Among other provisions, FDASIA amended the FFDCA to ensure accuracy and coordination of relevant FDA databases in order to identify and inform risk-based inspections under section 510(h).[6] FDASIA also changed the frequency of risk-based inspections of drug establishments from a fixed minimum inspection interval to a schedule established by FDA and in consideration of known safety risks of the establishments, such as its compliance and inspection history, the inherent risk of the drug manufactured, and records of any recalls linked to the establishment.[7] This change was designed to address the most significant public health risks by defining a risk-based inspection frequency for all sites, regardless of the domestic or foreign site of the facility.[8]

In 2017, Congress reauthorized the Generic Drug User Fee Amendments (GDUFA II), originally enacted in 2012, which requires generic API manufacturers to register, list, and pay fees to the FDA. A key feature is the pre-Abbreviated New Drug Application (pre-ANDA) program, which provides for "product development assistance and pre-submission and mid-review cycle meetings to help clarify regulatory expectations early in product development and during application review."[9] In FY 2018, FDA reported net collection of $493.7 million in human generic drug user fees (GDUFA fees), spent $477.3 million in user fees for the human generic drug review process, and carried a cumulative balance of $163.7 million forward for

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[4] FDA, *CY 2018 Annual Report on Inspections of Establishments,* (April 22, 2019*), available at* https://www.fda.gov/media/123480/download.
[5] Letter from Office of Legislative Affairs, U.S. Dep't of Health & Human Serv., to Hon. Frank Pallone, Jr., Chairman, H. Comm. on Energy & Commerce (Oct. 11, 2019).
[6] *Food and Drug Administration Safety and Innovation Act,* Public Law 112–144, 112th Congress (July 9, 2012) *available at* https://www.congress.gov/112/plaws/publ144/PLAW-112publ144.pdf.
[7] FDA *CY 2018 Annual Report on Inspections of Establishments,* (April 22, 2019*), available at* https://www.fda.gov/media/123480/download.
[8] FDA *Understanding CDER's Risk-Based Site Selection Model*, (Sept. 26, 2018), *available at* https://www.fda.gov/media/116004/download.
[9] FDA, *Pre-ANDA Program*, (last updated July 11, 2018), *available at* https://www.fda.gov/drugs/generic-drugs/pre-anda-program.

future fiscal years.[10] GDUFA user fees and non-user fee appropriations in FY 2018 supported 2,052 full-time equivalents (FTEs), including salaries and operational expenses, to support human generic drug activities.[11] The user fees are also used to support the costs of conducting associated drug inspections, including those conducted overseas. The fee for a foreign drug inspection includes an additional $15,000 for the extra costs incurred.[12]

Types of FDA Inspections

In June 2017, FDA's Center for Drug Evaluation and Research (CDER) and Office of Regulatory Affairs (ORA) entered into a concept of operations agreement[13] to integrate facility evaluations and inspections for human drugs.[14] The agreement outlines the responsibilities and the workflow for FDA's four types of inspections: Pre-Approval (product specific), Post-Approval (product specific, but risk-based), Surveillance (risk-based), and For-Cause (problem indicated) Inspections at domestic and foreign facilities.[15]

Before a new drug is approved, FDA conducts Pre-Approval Facility Evaluation and Inspections to determine if facilities are capable of manufacturing the drug pursuant to Current Good Manufacturing Practice (CGMP) requirements and ensure the accuracy and completeness of application data for a specific drug.[16] Potential risk information is also gathered and used in the post-approval processes to determine if a Post-Approval Inspection is needed.

Post-Approval Facility Inspections, like Pre-Approval Inspections, are product-specific but are completed after applications are approved, if an inspection is deemed necessary. These inspections focus on specific areas of concern that may have been identified during the pre-approval process. If the inspection team observes critical conditions or otherwise determines the need, the inspection may expand to a Surveillance Inspection based on a Drug Manufacturing Inspections Compliance Program. Post-Approval Inspections examine the process validation lifecycle and any changes in manufacturing changes that may have occurred after the product was approved.[17]

Surveillance Facility Inspections are geographically neutral and focus on facilities that manufacture approved marketed prescription and over-the-counter drug products, in addition to in-process materials or drug substances used in marketed drug products. Surveillance inspections monitor facility conformance to CGMP requirements and are manufacturing system-

[10] FDA, *FY 2018 GDUFA Financial Report,* (Oct. 2, 2019), *available at* https://www.fda.gov/media/131018/download.
[11] *Id.*
[12] *Id.*
[13] FDA, *Integration of FDA Facility Evaluation and Inspection Program for Human Drugs: A Concept of Operations* (June 6, 2017), *available at* https://www.fda.gov/media/107225/download.
[14] *Id.*
[15] Certain inspections may be carried out by investigators assigned to foreign offices under the FDA's Office of International Programs.
[16] FDA, *Integration of FDA Facility Evaluation and Inspection Program for Human Drugs: A Concept of Operations* (June 6, 2017), *available at* https://www.fda.gov/media/107225/download.
[17] *Id.*

based inspections.[18] Using facilities in the manufacturing catalogue, FDA's Office of Surveillance (OS) uses a risk-based selection model to generate a risk-based ranking priority of sites for inspection that are the highest risk facilities, regardless of the facility's geographic location.[19]

For-Cause Facility Inspections investigate concerns that have become known to FDA. These inspections are initiated by ORA, CDER's Office of Compliance, the Office of Surveillance, or the Office of Process and Facilities [20] and focus on examining specific problems, evaluation of conformance to CGMPs, and determine if enforcement action is needed.

When objectionable findings are observed in surveillance inspections, FDA documents the findings, issues a Form 483 and discusses the findings with the firm. Within 45 days, ORA completes and classifies the report into one of three categories: Official Action Indicated, Voluntary Action Indicated, or No Action Indicated. If the inspection is classified as Official Action Indicated, the report is reviewed by the Office of Manufacturing Quality (OMQ) to make a final classification and issue a decisional letter in the following 45 days. If OMQ downgrades the initial classification, ORA is notified, and the Office of Compliance issues the decisional letter no later than 90 days after the inspection was closed. If the inspection is classified as No Action Indicated or Voluntary Action Indicated, ORA issues a decisional letter within 90 days after the inspection closing.

When objectionable conditions are observed in For-Cause inspections, FDA issues a Form 483 with findings and discusses it with the firm. Within 45 days, ORA completes an establishment inspection report with a recommendation for review by the initiating office, which completes a final classification assessment in the following 45 days. Follow-up actions are completed within 6 months of the inspection closing.[21]

The FDA's Foreign Inspector Cadre

Inspections of drug manufacturing facilities in other countries may be conducted by staff on temporary duty assignments, in foreign offices, or by those who travel internationally.[22] The FDA also can recognize drug inspections conducted by foreign regulatory authorities that meet U.S. requirements through Mutual Recognition Agreements with the EU.[23] FDA expects the

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[18] *Id.*
[19] *Id*
[20] FDA, *Integration of FDA Facility Evaluation and Inspection Program for Human Drugs: A Concept of Operations* (June 6, 2017), ***available at*** https://www.fda.gov/media/107225/download.
[21] *Id.*
[22] FDA, *Statement from FDA Commissioner Scott Gottlieb, M.D., on the agency's global efforts to help assure product quality and transparency at foreign drug manufacturing facilities*, (Sept. 2018), *available at* https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-agencys-global-efforts-help-assure-product-quality-and.
[23] FDA, A New World for Pharmaceutical Inspections: The Mutual Recognition Agreement (Sept. 13, 2019), available at https://www.fda.gov/international-programs/international-arrangements/mutual-recognition-agreement-mra.

Mutual Recognition Agreements to provide more resources to higher risk inspection sites and increase efficiencies by avoiding duplication of inspections. [24]

As of October 25, 2019, ORA had 188 drug investigators qualified to conduct foreign drug inspections[25] and the Office of Global Policy and Strategy had 10 in-country full time employees qualified to conduct drug inspections. FDA informed Committee staff that they are bringing on 20 new inspectors and they are now at a deficit of 63 inspectors. With current staffing, FDA has the capacity to conduct about 1000 drug inspections a year.[26]

FDA informed Committee staff that in May 2017, they aligned their investigators with program areas instead of being based on geographic regions. The new structure focuses staff on specialty areas, resulting in 2000 field investigators being split among commodities. An inspector requires a year or two of experience before being qualified to conduct a foreign drug inspection. Foreign inspectors are typically GS-12 level or above.[27]

The FDA has approval for 25 total personnel in its field office in China and 18 total personnel in India. Currently, the agency currently has 6 drug inspectors in China with 3 drug inspector vacancy positions available. The FDA India office is staffed with 6 drug inspectors, 2 of which are detailees and 5 drug inspector positions remain open.[28]

Foreign Facilities Requiring Inspection

In FDA's October 11, 2019, response letter to the Committee's June 28, 2019 letter request for information, the FDA provided information regarding facilities requiring inspection from the May 2019 CDER Manufacturing Sites Catalog. FDA used this data to develop the prioritization list for FY 2020 Surveillance inspections. The catalog contains facilities that manufacture a human drug and are subject to routine or periodic inspections in fulfillment of FDA's statutory obligation for risk-based scheduling and performance of inspections under section 510(h) of the FFDCA. The catalog includes information primarily from the establishment registration system and other sources of FDA data useful for establishing a comprehensive list of manufacturing facilities producing APIs or FDFs for the United States.

[24] *Id.*
[25] FDA email to Committee staff (Dec. 5, 2019)
[26] FDA briefing to Committee staff (Nov.21, 2019).
[27] *Id.*
[28] *Id.*

Region	Total Number of Facilities	Number of Facilities Never Inspected	Number of Facilities Making API	Number of Facilities Making FDF	Number of Facilities Inspected Only Once for Firms Registered Before 1/01/2016	Median time between surveillance inspection (years)
Canada	138	-	18	95	33	2.5
China	340	9	204	124	94	2.6
EU	810	-	292	379	130	2.5
India	485	9	252	183	111	2.5
Japan	125	1	63	53	24	2.9
South Korea	58	5	9	41	30	1.8
USA	1754	63	157	1097	241	2.8
Other	313	20	86	206	68	2.7
TOTAL	4023	107	1081	2178	731	

Source: U.S. Department of Health and Human Services[29]

Approximately 80 percent of foreign drug inspections are conducted by one investigator and 20 percent are conducted by a team of two or more investigators. FDA provided the average time for their foreign inspections, which includes time spent preparing for, performing and reporting on the inspection, which means the time includes time spent outside the facility.

- The average time for a foreign API inspection is 95.6 hours.
- The average time for a foreign FDF inspection is 106.6 hours.[30]

Inspections of domestic U.S. manufacturers can be unannounced, but most international inspections must be announced beforehand by several months due to obstacles such as gaining country clearance and arranging for complex travel logistics. FDA does conduct short-notice foreign drug inspections when they are for-cause inspections and for a few surveillance inspections when in-country FDA staff is available.

The distinction between unannounced and announced inspections is significant and can affect the quality of the inspection, the accuracy of inspection reports, and whether a company maintains a consistent state of compliance between inspections. In 2014, the FDA instituted an initiative in India giving plants only short or no advance notice of inspections. As a result, the serious violations uncovered by inspectors rose by almost 60 percent.[31] The initiative was discontinued in July 2015. FDA told the Committee that the initiative was not extended based on a lack of protocols and evaluation criteria.[32]

[29] Letter from Office of Legislative Affairs, U.S. Dep't of Health & Human Serv., to Hon. Frank Pallone, Jr., Chairman, H. Comm. on Energy & Commerce (Oct. 11, 2019).
[30] *Id.*
[31] Katherine Eban, *Bottle X: Exposing Impurities in the Generic Drug Business*, Newsweek (July 2, 2019).
[32] Letter from Office of Legislative Affairs, U.S. Dep't of Health and Human Serv., to Hon. Frank Pallone, Jr., Chairman, H. Comm. on Energy & Commerce (Oct. 11, 2019).

FDA Warning Letters to Foreign Facilities

A warning letter is a notification from the FDA to a firm for violations of regulatory significance. For foreign firms, a warning letter can result in their products being placed on import alert by the FDA, effectively blocking their shipment into the U.S. An evaluation of data for FY 2018 based on drug CGMP warning letters posted by the FDA no later than Jan. 1, 2019 revealed:

- More than three times as many warning letters were issued to firms outside the U.S. compared with those issued to domestic firms.[33]

- Manufacturers in China received the most warning letters issued to sites in a single country.[34]

- Import alerts were associated with 48 of the 73 warning letters issued to sites outside the U.S. Firms in China, India, and Korea that received warning letters were the subject of 32 of the 48 import alerts associated with warning letters. In China, 21 of the 24 firms that received warning letters were subject to import alerts.[35]

Drug GMP Warning Letters Issued Regarding Sites Outside the U.S.[36]

Country / Geography	FY2013	FY2014	FY2015	FY2016	FY2017	FY2018	TOTAL
China	2	5	2	15	17	24	65
India	7	7	8	10	14	14	60
Europe	7	3	3	5	8	9	35
Canada	4	1	1		3	5	14
South Korea					2	9	11
Japan	2			1	3	3	9
Taiwan	1			2		3	6
Australia	1	1				3	5
Mexico		1				3	4
Brazil				2	1		3
New Zealand			1				1
Jamaica	1						1
Thailand			1				1
Singapore					1		1
Dominican Republic						1	1

[33] Barbara Unger, *An Analysis of FDA FY2018 Drug GMP Warning Letters*. (Feb.1, 2019) *available at* https://www.pharmaceuticalonline.com/doc/an-analysis-of-fda-fy-drug-gmp-warning-letters-0003.
[34] *Id.*
[35] *Id.*
[36] *Id.*

Import Alerts Associated with FY2018 Warning Letters[37]

	FY2018 Warning Letters	Number of Warning Letters Identifying Import Alerts
China	24	21
India	14	6
South Korea	9	5
Europe	9	5
Canada	3	3
Australia	3	2
Japan	3	1
Mexico	3	2
Taiwan	2	1
Dominican Republic	1	1

Earlier this month, the director of FDA's Office of Compliance at a generic drug industry conference noted that 73 percent of warning letters issued to all API manufacturers—foreign and domestic—over the past four years have included data integrity charges.[38] Data integrity includes incomplete, inconsistent, inaccurate, or falsified data.

Government Accountability Office Reports

The U.S. Government Accountability Office (GAO) has reported on the FDA's foreign drug inspection program for approximately twenty years and while improvements have been made during that time, many areas of concern have remained consistent, including staffing, number and quality of inspections, data integrity, and effectiveness of inspections.

In March 1998, the GAO issued a report entitled, "Food and Drug Administration: Improvements Needed in the Foreign Drug Inspection Program."[39] At that time, reports of seizures, deaths, and other problems suffered by Americans who took drugs that allegedly contained a poor quality ingredient that had been manufactured in a foreign country and imported by a U.S. pharmaceutical company raised concerns about the FDA's ability to ensure the safety and quality of the increasing volume of foreign-produced drugs imported into the U.S. GAO reported that almost 60 percent of FDA's foreign inspection reports were submitted later than agency standards, including half the reports that identified the most serious deficiencies in manufacturing quality.[40] FDA took four times longer than average to issue warning letters to foreign manufacturers. Inspection review personnel downgraded report classifications, most often based on foreign manufacturers promises to take corrective actions, even though the trustworthiness of the manufacturers was at issue. GAO also reported that FDA had obstacles

[37] *Id.*
[38] Zachary Brennan, *FDA Raises Concerns With API Manufacturers*, REGULATORY FOCUS, (Nov. 5, 2019), *available at* https://www.raps.org/news-and-articles/news-articles/2019/11/fda-raises-concerns-with-api-manufacturers.
[39] U.S. Gov't Accountability Office (GAO), *Food and Drug Administration: Improvements Needed in the Foreign Drug Inspection Program* (Mar. 1998) (GAO/HEHS-98-21).
[40] *Id.*

with inspections data management and tracking because they used multiple systems that did not communicate directly with each other.[41]

In 2007, the Committee asked GAO to examine FDA's efforts to improve its foreign drug inspection program. In 2008, GAO issued a report entitled, "Drug Safety: Better Data Management and More Inspections are Needed to Strengthen FDA's Foreign Drug Inspection Program," finding that human resource and logistical challenges unique to foreign inspections influenced how the FDA conducted inspections of foreign facilities. One factor was that FDA did not have a staff dedicated to conducting foreign inspections and instead relied on a cadre of volunteer inspectors to conduct foreign inspections.[42] GAO also found that FDA lacked access to trained, unbiased translators for FDA inspectors. FDA foreign inspections are technically complex, can be confrontational in nature, and require the review of numerous documents. FDA staff did not have an independent translator provided for inspections and instead sometimes relied on an English-speaking employee of the facility being inspected, which created a conflict of interest and raised questions about the accuracy of translation.[43] GAO also found that, unlike domestic inspections, which could be unannounced, logistical complications including visa applications and international sovereignty issues required that foreign inspections be pre-announced. Foreign facilities usually had more than one month notice of scheduled inspections. If problems were found during foreign inspections, FDA did not have the flexibility to extend length of the trip.[44]

In 2009, GAO added the FDA's oversight of medical products to its High Risk List because of the challenges FDA faced that threaten its ability to protect public health.[45] While progress has been made, challenges remain related to FDA's ability to respond to globalization and to help ensure the availability of drugs.[46] GAO publishes its High Risk List every two years and FDA's oversight of medical products has remained on the list ever since it was added in 2009.

In September 2010, GAO issued a report entitled, "Drug Safety: FDA Has Conducted More Foreign Inspections and Begun to Improve Its Information on Foreign Establishments, but More Progress is Needed." GAO found that FDA had started to respond to its 1998 and 2008 recommendations to conduct more inspections of foreign facilities and strengthen its data used to manage its foreign drug inspection program.[47] GAO reported that, because of the nation's

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[41] *Id.*
[42] GAO, *Better Data Management and More Inspections Are Needed to Strengthen FDA's Foreign Drug Inspection Program* (Sept. 2008) (GAO-08-970).
[43] *Id.*
[44] *Id.*
[45] GAO, *High Risk Series: Substantial Efforts Needed to Achieve Greater Progress on High-Risk Areas* (Mar. 2019) (GAO-19-157SP).
[46] GAO, *High-Risk Series: Progress on Many High-Risk Areas, While Substantial Efforts Needed on Others* (Feb. 2017) (GAO-17-317).
[47] GAO, *Drug Safety: FDA Has Conducted More Foreign Inspections and Begun to Improve Its Information on Foreign Establishments, but More Progress is Needed* (Sept. 2010) (GAO-10-961).

reliance on drugs manufactured overseas, it was urgent that FDA implement GAO's prior recommendations to protect public health better.[48]

In 2016, GAO published a report entitled, "Drug Safety: FDA Has Improved Its Foreign Drug Inspection Program, but Needs to Assess the Effectiveness and Staffing of its Foreign Offices."[49] GAO reported that FDA opened offices in China, India, Europe, and Latin America and increased the number of foreign inspections each year since FY 2009. However, nearly half of their authorized positions were unfilled, FDA had not assessed those offices' contributions to drug safety, and almost 1000 of the approximate 3000 foreign establishments remained uninspected.[50]

On June 28, 2019, the Committee requested that GAO conduct an updated review of FDA's foreign inspection program.[51]

The Effect of FDA Foreign Inspections on Patients

In 2008, the Committee held a series of hearings to examine the adequacy of the FDA's efforts to protect the U.S. from unsafe drugs. On April 29, 2008, the Committee held a hearing focused on the circumstances surrounding the contamination of Baxter International's heparin, a blood thinner drug that contained an adulterated active pharmaceutical ingredient from China, associated with deaths of American patients and, as of the hearing date, caused at least 785 severe allergic-like reactions.[52] Because FDA erroneously misidentified the plant, FDA believed it had conducted a pre-approval inspection of the API manufacturer of Baxter's heparin. However, the FDA did not conduct a Pre-Approval Facility Inspection of the facility that manufactured the contaminated API, even though the FDA did approve the manufacturer.[53] It is unknown if an FDA pre-approval inspection in 2004 would have prevented the outbreak from occurring, but it may have had a positive impact.[54] The FDA inspected the manufacturer in February 2008 after the Baxter heparin was linked to adverse events and determined the manufacturer was not capable of meeting current good manufacturing practices and was incapable of providing safe heparin API to the U.S.[55] The inspection was conducted before FDA's investigation found a man-made contaminant had been introduced in Baxter's supply chain in China, and was the cause of the adverse reactions in American patients.

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[48] *Id.*
[49] GAO, *Drug Safety: FDA Has Improved Its Foreign Drug Inspection Program, but Needs to Assess the Effectiveness and Staffing of its Foreign Offices* (Dec. 2016) (GAO-17-143)
[50] *Id.*
[51] Letter from Hon. Frank Pallone, Jr., Chairman, Hon. Greg Walden, Ranking Member, H. Comm. on Energy & Commerce, et al, to Hon. Gene Dodaro, Comptroller General (June 28, 2019).
[52] The Heparin Disaster: Chinese Counterfeits and American Failures: Hearings before the Subcommittee on Oversight and Investigations, of the House Committee on Energy and Commerce, 110th Cong., 2d Sess. (2008) (Opening Statement of Hon. Bart Stupak, Michigan).
[53] *Id.*
[54] *Id.*
[55] The Heparin Disaster: Chinese Counterfeits and American Failures: Hearing before the Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce, 110th Cong., 2d Sess. (2008) (Opening Statement of Hon. Bart Stupak, Michigan).

Beginning in July 2018, at least 15 recalls have been issued due to the presence of a cancer-causing contaminant in a variety of angiotensin II receptor blockers (ARB),[56] medications generally used to treat high blood pressure. The origins of this series of recalls appear to be two foreign drug manufacturing facilities: Zhejiang Huahai Pharmaceutical in China and Hetero Labs in India.[57] On September 28, 2018, drugs manufactured at Zhejiang Huahai were placed under an import alert by FDA to stop all APIs and FDFs from entering the U.S.[58] Before the recalls were issued, FDA inspection reports of these two facilities revealed serious problems.[59] For example, the inspector reported that Zhejiang Huahai in China had replaced test results that that showed drugs failed to meet U.S. standards with records that showed passing grades.[60] In May 2017, the inspector recommended that FDA send a warning letter to Zhejiang Huahai, one of China's largest exporters of pharmaceuticals.[61] The warning letter would have likely meant the manufacturer would not gain approval to make new generic drugs until it cleared up the list of problems.[62] However, four months later, FDA managers overruled the inspector and Zhejiang Huahai Pharmaceutical was allowed to avoid penalties and address the problems itself – potentially missing the chance to detect the cancer-causing contaminant more than a year earlier than it was.[63] On February 13, 2019, the Committee sent a bipartisan letter to FDA concerning a series of recalls involving drugs manufactured overseas that contained trace amounts of known carcinogens.[64] On June 28, 2019, the Committee sent bipartisan letters to GAO and FDA concerning FDA's foreign drug inspection program.[65]

[56] FDA, *Recalls, Market Withdrawals, and Safety Alerts* (recall information accessed Feb. 12, 2019) *available at* www.fda.gov/Safety/Recalls/default.htm.
[57] *Blood Pressure Drug Recall: FDA Investigates Foreign Plants That Made Drugs With Cancer-Causing Impurities*, USA TODAY (Jan. 25, 2019).
[58] FDA, *FDA updates on angiotensin II receptor blocker (ARB) recalls including valsartan, losartan and irbesartan* (last updated Nov. 13, 2019) *available at* www.fda.gov/Drugs/DrugSafety/ucm613916.htm; FDA, Import Alert 66-40, *available at*www.accessdata.fda.gov/cms_ia/importalert_189.html (last accessed Dec. 5, 2019).
[59] *Blood Pressure Drug Recall: FDA Investigates Foreign Plants That Made Drugs With Cancer-Causing Impurities*, USA TODAY (Jan. 25, 2019).
[60] *How a Tainted Heart Drug Made in China Slipped Past the FDA. Lag in U.S. recall highlights strain in global pharmaceutical supply chain*, BLOOMBERG, (Jan. 30, 2019).
[61] *Id*.
[62] *Id*.
[63] *Id*.
[64] Letter from Hon. Frank Pallone, Jr., Chairman, Hon. Greg Walden, Ranking Member, et al., H. Comm. on Energy & Commerce to Hon. Scott Gottlieb, M.D., Commissioner, FDA (Feb. 13, 2019).
[65] Letter from Hon. Frank Pallone, Jr., Chairman, Hon. Greg Walden, Ranking Member, et al., H. Comm. on Energy & Commerce to Hon. Gene Dodaro, Comptroller General, GAO (June 28, 2019).; Letter from Hon. Frank Pallone, Jr., Chairman, Hon. Greg Walden, Ranking Member, et al., H. Comm. on Energy & Commerce to Dr. Norman Sharpless, Acting Commissioner, FDA (June 28, 2019).